To suggest that drug treatment may take over for syringe exchange programs is to ignore these facts and to overlook a large body of knowledge suggesting the effectiveness of syringe exchange in reducing risk behavior (5, 6), preventing human immunodeficiency virus (HIV) infection (7), and, in some settings, preventing infection with HBV and HCV (8). Indeed, it appears that these programs may prevent HIV infection even while having no effect on HCV transmission. Seattle, Washington, may be an example of precisely these circumstances, with HIV incidence as low as 2 per 1,000 per year. Another notable example is Australia, where the extensive system of syringe exchange and distribution programs appears to have kept HIV transmission under control for several years even while annual HCV incidence is approximately 20 percent per year (9).

We would also argue against the assertion that exchange programs do nothing to change the underlying destructive activity of intravenous drug use. Several studies have shown that an exchange may be an ideal location for recruiting injection drug users into drug treatment (10–12), and nearly all US syringe exchange programs (97 percent) do provide drug treatment referral (13). Thus, it is conceivable that syringe exchange may have the net effect of *reducing* drug use in a community. Taken together, the evidence suggests that the public health benefits of a syringe exchange program are too great to discard them. We hope that HCV and HBV prevention efforts would not have to choose between syringe exchange and drug treatment but could work toward models that incorporate both types of interventions.

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RE: "ATTRIBUTABLE RISK IN PRACTICE"

In a recent *Journal* editorial, Walter (1) discussed the practice of attributable risk/fraction estimation when multiple risk factors have to be accounted for. He referred to two different approaches applied in subsequent articles (2, 3) of the same issue of the *Journal*. Benichou et al. (2) used the term "(adjusted) population attributable risk" for their risk parameter and applied standard adjustment procedures to incorporate the multifactorial nature of the problem, while Wilson et al. created the term "extra attributable fraction" for a risk parameter described in a special section of their paper entitled Attributable Fraction Methods (3, p. 417).

The terminological variety in these papers is typical for the entire field of attributable risk/fraction estimation in which some confusion about methods and terms persists (4–6). Wilson et al.'s (3) extra attributable fraction is identical to what we introduced as a "sequential attributable fraction" (7). The extra attributable fraction is the special sequential attributable fraction that results when the factor of interest is the last to be removed from a sequence in which all other factors have been removed earlier according to some prespecified order. That is, the extra attributable fraction should be interpreted as the proportionate reduction in disease risk obtainable when the given risk factor is eliminated after all other risk factors under consideration have already been eliminated. This is certainly different from Wilson et al.'s interpretation of the extra attributable fraction also referred to by Walter as representing "the effect of removing exposure to one risk factor, while leaving all other exposures unchanged" (1, p. 411). This latter interpretation is, however, suited for Benichou et al.'s (2) adjusted (population) attributable risks/fractions, whether for a single risk factor or a combination of risk factors.

We would also like to comment on Benichou et al.'s statement that "the PAR [population attributable risk] for the combination of two or more risk factors is usually less than the sum of the PARs for each risk factor" (2, p. 426), a situation that one might refer to as "supra-additivity" of attributable fractions (PARs). The opposite situation of "subadditivity" is more common than one might believe. For example, in a recent paper by Mezzetti et al. (8) in

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which adjusted attributable fractions for all singles, pairs, and triples of four risk factors were estimated by means of a logistic model, this phenomenon of subadditivity of adjusted attributable fractions was observed in more than half of all reported pairs of factors (11 of 20) in different models.

Finally, the nonadditivity of individual attributable fractions has been given considerable attention in the epidemiologic literature. Walter (9) and others (10, 11) showed that for conventional attributable fraction parameters, additivity is generally obtained only under conditions that seldom are fulfilled in practice, and Coughlin et al. (12) used additivity of attributable fractions to advocate the use of additive (without interaction terms) rather than multiplicative models. The property of additivity is obviously attractive for ease of interpretation of attributable fraction estimates and especially useful in tort-law liability situations. Therefore, readers of the *Journal* should note our definition of the concept of average attributable fraction for multifactorial risk attribution in epidemiology (7). In the multifactorial situation, this approach provides the unique solution (under reasonable conditions) to the problem of dividing the total proportion of cases attributable to the entire set of exposures under study into exposure-specific components. These average attributable fractions for the single exposures in the set of factors under study do indeed sum to their combined attributable fraction. Further discussion and justification of this approach is provided elsewhere (7, 13–15).

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DR. WALTER REPLIES

The helpful comments from Eide and Gefeller (1) regarding my editorial (2) underscore the need for clarity when discussing attributable risk estimates. In particular, one must define which factors or combination of factors are being evaluated, state which other factors are to be taken into account, and specify the implied changes in risk exposure that are envisaged. Several typical possibilities exist, as follows.

First (case A), epidemiologists, particularly those contemplating preventive interventions, will wish to consider the number of cases associated with a specific risk factor, in an environment in which other risk exposures exist but may not change as a result of the intervention. For example, smoking cessation campaigns are directed primarily at the elimination of smoking. Secondary effects on other risk factors, such as exercise and diet, may occur but are not the target of the intervention. Here one should calculate the attributable risk for the factor in question (smoking) by regarding it as the *first* exposure to change in the population, leaving the other exposures unchanged. If they are available, data on other exposures can become part of the calculation, in which empirical methods (3) or a logistic regression model (4) is used.

Second (case B), Wilson et al.'s approach (5) considers the *extra* attributable risk for a factor. It is intended to indicate the effect of eliminating an exposure assuming that the other factors remain unchanged. In contrast to case A, however, the factor in question is implicitly assumed to be the *last* to be taken into account, as pointed out by Eide and Gefeller (1). Wilson et al.'s approach calculates the difference from the summary attributable risk for all factors and the summary attributable risk for all factors except the one under study.

An example would be if one wanted to estimate the proportion of disease cases associated with an occupational toxin while recognizing that some employees smoke. In a compensation or tort case, the employer would argue that the smoking is the employees' responsibility and that the toxic hazards of the job are secondary to those of smoking.

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